Assessment of Personality Disorder in Adult ADHD Using Data from a Clinical Trial of OROS Methylphenidate (OROS MPH)

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ABSTRACT:

Background: Studies have reported high comorbidity of personality disorder and adult ADHD. However, assessment of personality disorder is problematic and none have rigorously confirmed this observation with measures of concurrent validity.

Methods: 47 patients entered a double-blind trial of OROS MPH after administration of the Wisconsin Personality Inventory (WISPI-IV) and the SCID-II. At discharge, all information was reviewed to produce a final consensus personality diagnosis. Patients were separated into three post hoc categories: PDnegative (no personality disorder), PDpositive (subjects meeting diagnostic criteria for one disorder), and PDplus (subjects meeting diagnostic criteria for ≥2 disorders).

Results: 45% of subjects had a personality disorder on the final assessment versus 62% (SCID-II) and 33% (WISPI-IV): 11% cluster A, 17% cluster B and 30% cluster C. Compared to the final assessment, the WISPI-IV identified PDnegative subjects with sensitivity = .92 and specificity = .67 and PDplus subjects with sensitivity = .40 and specificity = 1.00. The SCID-II identified PDnegative subjects with sensitivity = .64 and specificity = .90 and PDplus subjects with sensitivity = .90 and specificity = .84. There was a significant correlation between the number of SCID-II items endorsed by each subject and their WISPI-IV average z-score (r=.67, df=46, p<.001).

Conclusions: All three systems detected personality disorder in a large proportion of patients. The WISPI tended to under-estimate personality disorders while the SCID-II over-estimated them. The self-administered WISPI-IV would be more practical in a multicenter clinical trial to provide an estimate of personality disorder.

INTRODUCTION

Light therapy has been demonstrated useful in treating SAD. The seminal article by Rosenthal et al (1984) hypothesized about the depressogenic effects of melatonin and described preliminary findings about the effects of artificial light therapy. Since that time, research has supported this observation and expanded to conditions other than SAD such as problems with jet-lag and shift work. A particular area of interest is the relationship between SAD and other affective disorders. It is probable that even within SAD studies, subjects do not all suffer from pure SAD, but most studies do not indicate the degree of overlap in their samples. For example, patients with major depressive disorder often have seasonal variations with winter being the season with the greatest risk for depression (Kasper et al 1990).

Photosensitive retinal ganglion cells that project from the retina to the suprachiasmatic nucleus, intergeniculate leaflet and olivary pretectal nucleus (Gooley et al 2003) are probably responsible for the melatonin suppression associated with light therapy. It appears that these cells respond most strongly to wavelengths of ~480nm. This understanding has led to the development of blue light therapy for SAD.

While blue light treatment of SAD has proven effective in prior trials, the present study was an improvement in three ways: 1) The use of bright red light as placebo rather than the commonly used dim red light. 2) The impact of incomplete summer remission on treatment outcome was assessed. 3) An open-label, follow-up period was included.

METHODS

This was a 3-week, parallel, controlled, double-blind trial of bright blue light in the treatment of SAD conducted during January and February 2006. Subjects were categorized post hoc into those with evidence of comorbid major depression based on subjects' past history and/or ongoing use of antidepressant medication (SAD or SAD+MDD). Although subjects could not be blind regarding the color of their light panel, they were blind regarding the hypothesis that blue would be effective and red ineffective. All subjects who completed the double-blind trial were given an opportunity to enter into a 4-week open-label trial of blue LED light treatment.

Patient eligibility:

- Met criteria for Seasonal Affective Disorder plus a baseline SIGH-SAD score ≥20
- Outpatients 18 years or older
- General good health without photosensitive conditions
- No recent use of light therapy and no past failed treatment of light therapy

Equipment:

The light treatment units were designed and produced by the sponsor of this study: Apollo Light Systems, Orem, Utah. The active unit was a 470 nm blue LED light unit and the placebo unit was a 650 nm red LED unit. While the photon densities of the two panels were not the same, their visual intensities were very similar. The brightness of the red panel increased its credibility as a placebo treatment.

Data analysis:

Efficacy in the double-blind period was assessed using repeated measures-ANOVA (baseline to end-point) for continuous variables and Fisher's exact test for categorical variables (LOCF). Efficacy in the open-label period was assessed two ways: 1) Comparing the open-label outcome with baseline. 2) Separate comparisons of open-label to double-blind for the two treatment groups using paired t-test for continuous variables and Fisher's exact test for categorical variables.

RESULTS

Baseline:

As seen in Table 1, the two double-blind treatment groups were very similar except for age.

Table 1: Characteristics at baseline for both double-blind groups and all subjects entering open-label treatment.

	Red-Light	Blue-Light	Open-Label
N	15	15	25
Age (years)	39.5±9.9	51.1±12.3	45.6±12.5
Female n(%)	13(87%)	10(67%)	19(76%)
HAMD-17	19.7±5.1	20.3±3.7	20.0±4.7
SIGH-SAD	34.1±5.9	34.1±5.6	33.9±6.0
SAD+MDD	4(27%)	7(47%)	8(32%)

Double-Blind:

Blue-light therapy proved significantly more effective than red-light in every outcome measure except SIGH-SAD scores: HAMD-17 ($F_{1,26}=4.52$, $p=.043$); SIGH-SAD ($F_{1,26}=2.19$, $p=.15$); CGI-I (Fisher's exact test $p=.01$); CGI-S (Fisher's exact test $p=.01$).

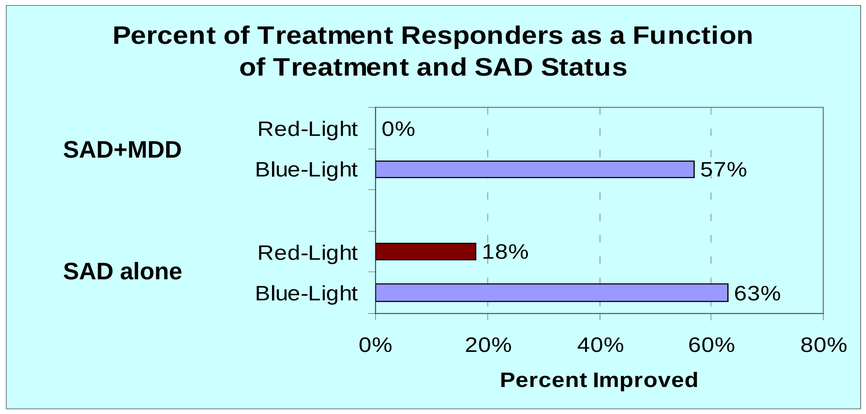
Table 2: Improvement in depressive symptoms during the double-blind phase as a function of treatment.

	Red-Light	Blue-Light	p-Value[a]
N	15	15	
Improvement in HAM-D scores: mean±sd (%) improvement over baseline			
HAMD-17	6.0±3.9 (32%)	10.1±5.3 (51%)	.05
SIGH-SAD Total	10.2±10.7 (21%)	15.7±9.6 (40%)	.15
Categorical Improvement: N (%) improved			
CGI-I ≤2	2 (13%)	9 (60%)	.01
CGI-S ≤3	2 (13%)	9 (60%)	.01
HAMD-17[b]	2 (13%)	8(53%)	.05

a) p-Values were calculated (LOCF) using a repeated measures ANOVA procedure for continuous variables and the Fisher exact test for categorical variables.
b) Subjects experiencing at least a 50% improvement in HAMD-17 scores were categorized as improved.

SAD alone and SAD+MDD differences:

On the HAMD-17, the 19 subjects with pure SAD improved an average of 32% in the red-light arm and 61% in the blue-light arm, a difference that approached significance (p=.08). Further, 63% of them met CGI-I criteria for improvement in the blue-light arm, while 18% improved in the red-light arm (Fisher exact test =.074). The 11 subjects with SAD+MDD improved an average of 30% in the red-light arm and 40% in the blue-light arm, a difference that was not significant (p=.70). However, 57% of them met CGI-I criteria for improvement in the blue-light arm while none improved in the red-light arm (Fisher exact test =.194).



Open-Label:

All subjects who completed the double-blind trial were given an opportunity to enter into a 4-week open-label trial of blue-light treatment. Change from baseline to endpoint was dramatic for these subjects. Subjects improved 64% on HAMD-17 scores ($F_{1,21}=120.6$, $p<.001$) and 73% on SIGH-SAD scores ($F_{1,21}=112.7$, $p<.001$). As seen in Table 3, subjects from the placebo group showed statistically significant improvement over the double-blind period in all reported measures. In contrast, subjects from the blue-light group showed minor, nonsignificant improvement in all measures. By the end of the open-label phase, the two groups did not differ significantly on any measure.

Table 3: Outcome measures at baseline, double-blind and open-label for subjects entering the open-label phase. Data are presented using LOCF within each phase.

	Baseline	Double-Blind	Open-Label	p-Value[a]
Red-Light Group N=13				
HAMD-17	19.4±5.3	13.2±5.7	6.5±7.9	.022
CGI-I ≤2	na	2(15%)	11(85%)	.001
Blue-Light Group N=12				
HAMD-17	20.6±4.0	9.8±6.7	8.0±7.1	>.50
CGI-I ≤2	na	8(67%)	10(83%)	>.50

a) p-Values compare open-label with double-blind scores (LOCF). Continuous data were assessed using paired t-tests and categorical data were assessed using the Fisher exact test.

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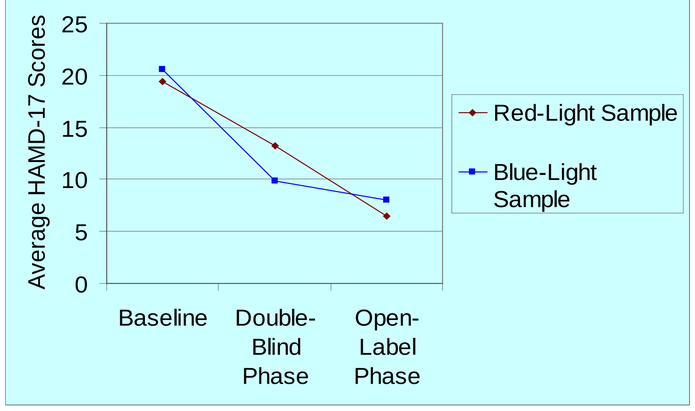
Fig 1. Average HAMD-17 Scores for the Two Double-Blind Treatment Groups During the Baseline, Double-Blind and Open-Label Treatment Phases



SAD alone and SAD+MDD differences:

Both subjects with SAD alone and SAD+MDD showed statistically significant improvement by the end of the open-label phase. These analyses include all subjects with any blue-light treatment (including those who did not enter the open-label period). On the HAMD-17 the 16 subjects with SAD alone improved 71% over baseline (p=.001), while the 12 subjects with SAD+MDD improved 56% (p=.005)(LOCF). Similarly, 88% of subjects with SAD alone met CGI-I criteria for improvement while 67% of subjects with SAD+MDD alone met CGI-I criteria for improvement (LOCF).

Adverse Events and Side Effects:

Blue LED light therapy was similar to red LED light therapy in the incidence of adverse events and side-effects. In the course of this study (both double-blind and open-label phases) 10 subjects reported a total of 17 adverse events or side effects during blue-light therapy. One subject discontinued treatment because of photosensitivity. This subject was in the blue-light arm, and left the study after one week double-blind treatment. There were five reports of headaches; two reports each of sleep disturbance and eye irritation; and one report each of: light headed/dizzy, upper respiratory infection, sunburn, photosensitivity, nausea, odd dreams, memory problems, and dysphoria. Nine of these problems were described as mild and eight were described as moderate.

CONCLUSIONS

- Blue-light therapy proved effective in treating Seasonal Affective Disorder.
- Bright red-light therapy proved to be an effective placebo condition, suggesting that future research should consider it in place of dim red-light as a placebo.
- Incomplete summer remission (SAD+MDD) was associated with lower responses to treatment in the double-blind period. However, 67% of these subjects had responded to treatment by the end of the open-label condition.
- Side effects were similar in the two treatment conditions and similar to past bright-light studies with one subject discontinuing treatment because of photosensitivity.
- These results support biological studies implicating photosensitive retinal ganglion cells and melatonin suppression in the treatment of seasonal affective disorder.
- This study was underpowered to fully address potential differences between the SAD and SAD+MDD samples. Larger studies are needed.

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